

**REMARKS**

Claims 1-6 are pending in this application. By this Amendment, claim 1 is amended.

No new matter is added.

**I. Claim 1 Satisfies Formal Requirements**

Claim 1 is objected to for informalities. By this Amendment, claim 1 is amended responsive to the objection. Withdrawal of the objection is respectfully requested.

**II. The Claims Define Patentable Subject Matter**

Claims 1-6 are rejected under 35 U.S.C. 103(a) over EP 1 182 250 to Otomo et al. (hereinafter "Otomo") in view of U.S. Patent No. 5,144,854 to Bertholdt and U.S. Patent No. 4,994,384 to Prather et al (hereinafter "Prather"). The rejection is respectfully traversed.

None of the applied references teaches or would have rendered obvious a single-cell operation supporting robot that includes a means for the transportation of a sample injection device which transports a sample injection means for injecting a sample into a single-cell relatively to and from the microwell for storing cells at four variances (x, y and z axes and an angle  $\theta$  versus an xy-plane) from claim 1, and a cell transport means which transports a cell holding means for holding a single-cell with respect to and from each of the microwells for storing cells, the single-cell stimulating device and sample injection means at the four variances (x, y and z axes and an angle  $\theta$  versus the xy-plane), as recited in independent claim 1.

The Office Action asserts that Otomo discloses a single-cell operation supporting robot used to inject amphibian oocytes with liquid comprising a means for transportation of a sample injection device at Fig. 1 and paragraphs [0016]-[0017]. However, the apparatus for microinjection of samples into amphibian oocytes disclosed in Otomo relates to an automated apparatus for microinjection of samples into oocytes of an amphibian, such as frogs. Thus, the size of the oocytes of interest is in the order of 1,000  $\mu\text{m}$ , which is a comparatively large

size (see, e.g. Otomo, paragraphs [0001] and [0002]). To the contrary, the single-cell operation support robot of the claimed invention is for supporting single-cell operation works that inject various samples into single-cells having various sizes, for example, in the order of 10  $\mu\text{m}$ .

In addition, the apparatus of Otomo can rapidly produce, in mass production, oocytes having almost the same quality (see, e.g., Otomo, paragraph [0038]), whereas the apparatus of the claimed invention can handle single-cells that have different qualities and sizes of some tens of micrometers. In this regard, the apparatus of Otomo and the apparatus of the claimed invention are essentially different in terms of qualities and the sizes of the cells to be handled.

The apparatus of Otomo merely has a driving means for moving a relative position of a tray for holding a plurality of amphibian oocytes to an injection needle for injecting a sample into the amphibian oocytes, and controlling means for controlling the relative positions between the tray and the injection needle in a three-dimensional direction (see, e.g. Otomo, paragraphs [0011]-[0013]). The controlling means of Otomo determines a reference point for the injection operation, sets moving distance and depth of the injection needle only for the vertical direction against a plane of the tray from the reference point to the position of injection sample and controls the depth in the Z-axis direction in the order of several tenths of a millimeter (see, e.g., Otomo, paragraph [0034]). This arrangement allows the sample injection apparatus of Otomo to be able to produce oocytes or a group of oocytes having substantially the same position from which the sample has been injected. In other words, the sample injection apparatus of Otomo merely controls the injection of the samples according to the information of the three-dimensional positions in order to improve the efficiency of the sample injections. Accordingly, Otomo neither teaches nor would have rendered obvious a means for the transportation of a sample injection device which transports a sample injection means with respect to and from the microwell for storing cells at the four variances and a cell

transportation means which transports a cell holding means for holding a single-cell with respect to and from each of the microwell for storing cells, the single-cell stimulating device and the sample injection means at the four variances, as recited in independent claim 1.

By using the claimed means for the transportation of the sample injection device and the claimed cell transportation means, the single-cell operation supporting robot of the claimed invention can inject the samples with an operation precision of 1  $\mu\text{m}$  or less. The (precision) of the claimed invention is thus remarkably improved as compared to that of Otomo.

The invention of Otomo and the claimed invention also differ in their objects to be solved. The apparatus of Otomo aims to improve the injection efficiency and to timely produce oocytes of an amphibian that have comparatively large sizes and the same quality and are injected samples at particular positions at particular depths. To the contrary, the single-cell operation supporting robot of the claimed invention aims to treat many single-cells by individually discriminating them throughout a series of single-cell operations including, for example, the holding, transportation and arrangement of single-cells on a microscope stage, the injection of various samples such as genes and drugs into each single-cell, the application of stimulations to each single-cell, and the measurement of the cell responses and the dynamic behavior of cellular molecules, which single-cell operations are difficult to be carried out by a single person. Thus, the invention of Otomo and the claimed invention are different in terms of the object to be solved by the irrespective inventions.

Further, Bertholdt and Prather do not remedy the above-described deficiencies of Otomo. One of ordinary skill also would not have modified the apparatus of Otomo to include the features of the apparatuses of Bertholdt and Prather as alleged in the Office Action. For example, the Office Action asserts that 1) one of ordinary skill in the art would substitute the ccd camera and monitor set up of Otomo with the microscope of Bertholdt

"because doing so would have resulted in nothing more than a simple substitution of known methods for positioning an injection device relative to a living cell with a reasonable expectation of success," and 2) it would have been obvious to one of ordinary skill in the art at the time of the invention "to incorporate into the device of modified Otomo, a cell holding pipette as taught by Prather in order to allow for the easier transfer of fluid into the individual cells/oocytes." However, the sample injection apparatus of Otomo aims to improve sample injection efficiency and to have a rapid production of a group of oocytes. There would have been no motivation to add an additional element, such as a microscope and a manual operation means described in Bertholdt and a cell holding pipette used in the micromanipulation of bovine cells described in Prather, because such modification would likely complicate Otomo's apparatus and thus deteriorate the efficiency. Thus, one of ordinary skill in the art would not have modified the apparatus Otomo as alleged in the Office Action.

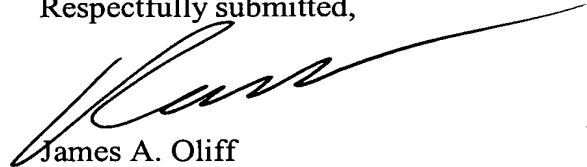
Thus, for at least these reasons, independent claim 1 is patentable over the applied references. Further, claims 2-6, which depend from claim 1, are also patentable over the applied references for at least the reasons discussed above, as well as for the additional features they recite. Withdrawal of the rejection is thus respectfully requested.

### **III. Conclusion**

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance. Favorable reconsideration and prompt allowance are earnestly solicited.

Should the Examiner believe that anything further would be desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact the undersigned at the telephone number set forth below.

Respectfully submitted,



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Attachment:  
Petition for Extension of Time

Date: July 6, 2009

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